Angiotensin Receptor Blockers Should Be Regarded as First-Line Drugs for Stroke Prevention in Both Primary and Secondary Prevention Settings

Yes

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Each year, stroke is responsible for 5.5 million deaths worldwide and the loss of >49 million disability-adjusted life-years. Interventions that effectively and efficiently prevent stroke therefore exert major economic, societal, and personal impact. An important modifiable risk factor for stroke is blood pressure, abnormal levels of which account for 54% of the worldwide burden of cerebrovascular disease.1 Unequivocal evidence supports blood pressure-lowering for preventing stroke both in primary and secondary prevention settings.

Although most systematic reviews, including the series of analyses produced by the Blood Pressure Lowering Treatment Trialists’ Collaboration, suggest that all major classes of antihypertensive drugs prevent stroke to a similar degree, important exceptions do exist. The risk–benefit profile of α-blockers and β-blockers, to cite 2 examples, have recently been questioned by evidence from randomized trials.2,3 In addition, many new trials of angiotensin receptor blocker classes (ARBs) for cardiovascular protection have now been completed but have not yet been integrated into existing systematic review databases.

Although mixed signals exist such as the recently reported Prevention Regimen for Effectively Avoiding Second Strokes Study (PRoFESS),4 most ARB trials have demonstrated the efficacy of this newer class of antihypertensives for preventing stroke. Settings in which broad cardiovascular protection with ARBs have now been documented include patients with primary hypertension with or without target organ damage; in acute ischemic stroke or longer-term in the aftermath of stroke; in patients with coronary artery disease or chronic heart failure; and after acute myocardial infarction. In the recently published Ongoing Telmisartan Alone and in Combination with Ramipril Global End point Trial (ONTARGET),5 the ARB telmisartan was deemed statistically equivalent to ramipril for preventing cardiovascular events in patients with vascular disease or diabetes; in a similar population, ramipril was previously found to be highly effective at preventing stroke (relative risk, 0.68; 95% CI, 0.56 to 0.84; P = 0.0002).6 In ONTARGET, telmisartan was slightly but not significantly more effective than ramipril for stroke prevention (relative risk, 0.91; 95% CI, 0.79 to 1.05).5 Although no placebo group was included in ONTARGET, an investigator-initiated pooled analysis of the placebo-controlled telmisartan portion of PRoFESS and another placebo-controlled ARB megatrial (the Telmisartan Randomized Assessment Study iNtolerant subjects with cardiovascular Disease [TRANSCEND]) suggested that telmisartan reduces the risk of major cardiovascular events by approximately 10% (OR, 0.91; 95% CI, 0.85 to 0.98) with greater efficacy seen after 6 months of therapy (OR, 0.85; 95% CI, 0.78 to 0.92).4,7

When choosing among specific blood pressure-lowering classes, 2 other considerations are cost-effectiveness and tolerability. In terms of the latter, pharmacoepidemiologic data suggest that patients who are prescribed ARBs are much more likely to remain on them than patients who are prescribed other antihypertensive classes; this is an important consideration because nonadherence is a strong risk factor for both vascular events and mortality.8,9 In terms of the former, several ARBs are either already generic or expected to become generic in the near future and formal cost-effectiveness studies demonstrate good economic usefulness even in the “brand name” era.10 In summary, ARBs should now be viewed as first-line agents for stroke prevention, taking their place among other effective interventions such as thiazide diuretics, calcium channel blockers, angiotensin-converting enzyme inhibitors, statins, and antiplatelet drugs.

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